REMARKS

Applicants' remarks to overcome the claim rejection under first paragraph of 35 U.S. C 112

The examiner has acknowledged that the present invention may be practiced analogously for the several antimetabolites disclosed and that, therefore, the number of species within the genus represented by the generic claim should not be at issue. Please see the interview summaries for Telephone Interviews on 10/16/09 and 12/8/09.

However, the examiner had raised the question whether the applicants have reasonably showed the possession of the claimed genus and rejected, for lack of written description to support, claims 51, 54-74 and 76-90 which recite or inherit the limitation, "an oligonucleotide comprising at least two CpG moieties and a **nucleoside antimetabolite** covalently linked to the oligonucleotide."

Applicants respectfully request that this rejection be reconsidered and withdrawn in view of the remarks that follow, scientific citations and the other documentation submitted herewith, which show that the applicants were in possession of the claimed genus, based on their disclosure of a combination of relevant functional characteristics coupled with a correlation between function and structure well known in the prior art

Section 112, paragraph 1 of the Patent Act sets for the written description requirement as follows:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or which it is nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out this invention.

To satisfy the written description requirement, "the applicant does not have to utilize any particular form of disclosure to describe the subject mater claimed, but the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." In re Alton, 76 F.3d 1168, 1172 (Fed. Cir. 1996). In other words, the applicants must convey with

reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." Vas-Cath Inc., 935 F.2d at 1563-64 (Fed. Cir. 1991).

Whether the written description requirements is satisfied is a fact-based inquiry that will depend on the nature of the claimed invention, Enzo, 23 F.3d at 963, and the knowledge of the one skilled in the art at the time an invention is made and a patent application is filed.

The Guidelines for Examination of Patent Application under 35 U.S.C Section 12, first paragraph "Written Description" requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) (Guidelines), an accurate description of the law for examining patent applications, and a persuasive authority, provide further guidance for determining whether the written description requirement is met for claims drawn to a genus. The Guidelines state:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species ... by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.
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> * * *
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> Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For invention in an unpredictable art, adequate written description of a genus

> which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

Guidelines, 66 Fed. Reg. at 1106.

The Office Actions and the Advisory Action highlighted much of the foregoing general requirements for written description. However, the instant patent application is akin to the patent application in Capon v. Eshha, 418 F.3d 1349, 1358 (Fed. Cir. 2005).

In Capon, the Federal Circuit has elaborated on the written description requirement under first paragraph of 35. U.S.C. 112. In Capon, the Federal Circuit held that "what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject mater." Id.

The invention in Capon involved "chimeric DNA that encodes single-chain chimeric proteins for expression on the surface of the cells of the immune system, plus expression vectors and cells transformed by the chimeric DNA. The Federal Circuit held that the Board of Patent Appeals and Interference erred in holding that the written description requirement was not met because the disclosure failed to "reiterate the structure or formula or chemical name of the nucleotide sequences of the claimed chimeric genes."

The Federal Circuit held in Capon that the prior art contained "extensive knowledge of the nucleotide structure of the various immune-related segments of DNA," including "over 785 mouse antibody DNA light chains and 1,327 mouse antibody DNA heavy chains." Id. at 1355.

Similarly to the patent application in Capon, the claim element "nucleoside antimetabolite" of the present application was well known to the one skilled in the art of preparing oligonucleotides with modified nucleosides at the time this application was filed.

Nucleoside is defined as a molecule a nitrogenous base and a pentose sugar (Lehninger – Principles of Biochemistry). The online encyclopedia (Wikipedia) provides the following description for nucleoside antimetabolite.

> An **antimetabolite** is a chemical that inhibits the use of a metabolite, which is another chemical that is part of normal metabolism. Such substances are often similar in structure to the metabolite that they interfere with.

> Antimetabolites can be used in cancer treatment,[3] as they interfere with DNA production and therefore cell division and the growth of tumors. Because cancer cells spend more time dividing than other cells, inhibiting cell division harms tumor cells more than other cells.
> Anti-metabolites masquerade as a purine (azathioprine, mercaptopurine) or a pyrimidine - which become the building blocks of DNA. They prevent these substances from becoming incorporated in to DNA during the S phase (of the cell cycle), stopping normal development and division.

The Paragraph 0076 of the instant patent application also provides the description for "nucleoside antimetabolite." Moreover, the Appendix entitled "**Scientific Publications describing the use of antimetabolite nucleoside prior to the filing of the Patent Application No. 10/768,996"** attached to this " Remarks" section also lists 36 peer-reviewed scientific publications discussing various antimetabolite nucleosides known in the art prior to filing of the instant patent application. A variety of antimetabolite nucleosides were known in the art prior to the filing of the instant application.

Therefore, the generic claim, claim 51 of this invention, does not depend on the use of any particular antimetabolite nucleosides *per se* in the treatment of cancer.

Rather, claim 51 embodies what the inventors have invented: a new genus of composition comprising an oligonucleotide with at least two CpG moieties and a nucleoside antimetabolite covalently linked to the oligonucleotide.

Claim 74 limits claim 51 to a special structural motif of this composition, and claim 89 discloses the method of making the nucleotide of claim 51.

Thus as per the standard for written description set forth by Federal Circuit in Capon, one of skill in the art would recognize that the applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed for an oligonucleotide with at lease two CpG moieties and a nucleotide antimetabolite covalently linked to the oligonucleotide.

For all the reasons presented above, it is respectfully submitted that the claims at issue are patentable. and that rejection with respect to claims 51, 54-74 and 76-90 should be withdrawn.

CONCLUSION

The Applicants have shown that the generic claims fulfill the written description requirements and that the applicants were in possession of the invention in accordance with the published guidelines and the guidance provided by the Examiner.

Furthermore, the Applicants invented a completely novel approach for fighting cancer and disclosed compelling experimental data. They have also disclosed how this technology may be replicated to target various forms of cancer by utilizing a variety of antimetabolites with cancer-fighting properties.

A Notice of Allowance for the claims presented, including the generic claims, is respectfully requested. Kindly contact the undersigned representative for any matter still outstanding in the case to put it into a condition for allowance.

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Respectfully submitted,

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